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Cognitive rehabilitation for individuals with multiple sclerosis does not have defined treatment protocols but the current literature expresses that treatment does show improvement

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Review date:(usually 2 years later)

CLINICAL SCENARIO: Cognitive impairment is a common symptom of many clients who have multiple sclerosis (MS). This can impact an individual's everyday function when trying to remember to go to a doctor's appointment or recalling when to take their medication. People with MS experience approximately 40-60% of cognitive problems in varying severities. Some of the cognitive problems include: slowed processing of information, difficulty with retrieving words, concentration, executive function, memory, and decreased judgment, abstract reasoning becomes more difficult, and verbal fluency is reduced. The writer wanted to investigate what amount of cognitive rehabilitation is needed in order for there to be functional outcomes in daily occupations.

FOCUSSED CLINICAL QUESTION: Does cognitive rehabilitation improve functional outcomes in individuals with multiple sclerosis?

SUMMARY of Search, 'Best' Evidence' appraised, and Key Findings:

- The researcher found 5 studies that matched the inclusion/exclusion criteria below.
- Groverover, Y. et al. (2008) was shown to have the "best" evidence with a cohort/mixed design with both a within- and between-subject. The study examined how a generation technique compared to a provided condition improved learning and memory through tasks like meal preparation and managing finances for people with MS.
- Gentry, T. (2008) examined the functional performance of people with MS who used PDAs as cognitive aids.
- Tesar, N. et al. (2005) examined the efficacy of a computer based training program that included compensatory techniques for everyday life. The study also subjectively looked at how the training program is relevant to everyday life.
- Vogt, A. et al. (2009) examined the use of doing two different training schedules on a computer based program called *BrainStim* to improve working memory for

people with MS.

- Shevil, E. & Finlayson, M. (2009) performed a process evaluation of “Mind over Matter” which is a self-management cognitive program for individuals with MS.

CLINICAL BOTTOM LINE: Self-generation compared to a provided condition can improve the recall of information and activities of daily living significantly for people with MS.

Limitation of this CAT: This critically appraised topic was reviewed by course faculty member only. This is not a complete and exhaustive literature research of this topic nor is the writer considered an expert on this topic.

SEARCH STRATEGY:

- The following databases were included in my search: CINAHL, Medline, OT Seeker, American Journal of Occupational Therapy (AJOT) through The American Occupational Therapy Association, Inc. (AOTA)

Terms used to guide Search Strategy:

- **Patient/Client Group:** multiple sclerosis, neurological condition
- **Intervention (or Assessment):** cognitive rehabilitation, computer based, intervention, cognitive therapy, memory
- **Comparison:** N/A
- **Outcome(s):** functional outcomes, activities of daily living

Table 1: Summary of databases searched and search terms used.

Databases and sites searched	Search Terms	Limits used
CINAHL	Multiple sclerosis, cognitive rehabilitation	Both words had to be in an abstract.
CINAHL	Multiple sclerosis, computer-based, intervention	Publications from 2000 to present.
Medline	Multiple sclerosis (rehab therapy), cognitive therapy (methods)	Used the search key to explode MS and cognitive therapy

INCLUSION and EXCLUSION CRITERIA

- *Inclusion:*
 - Studies must be in English.
 - Studies must be on cognitive rehabilitation for people with MS.
 - Studies needed to be currently published within approximately the last 10 years (2000 to present).
 - Studies generated from other countries than US.
- *Exclusion:*
 - Studies that are on cognitive rehabilitation for other conditions.
 - Studies that included other conditions.
 - Studies that were non English.

RESULTS OF SEARCH:

Five relevant studies were located and categorised as shown in Table 1 (based on Levels of Evidence, Evidence-Based Rehabilitation, (2008))

Table 2: Summary of Study Designs of Articles retrieved

Study Design/ Methodology of Articles Retrieved	Level	Number Located	Author (Year)
Randomized Control Trial	1b	1	Tesar, N. et al. (2005)
Cohort/Mixed-design with both a within- and between-subject factor	2b	1	Goverover, Y. et al. (2008)
Cohort design studies with no control group	2b	2	Gentry, T. (2008) Vogt, A. et al. (2009)
Cohort /qualitative design study	2b/NA	1	Shevil, E. & Finiayson, M. (2009)

BEST EVIDENCE

The following study/paper was identified as the 'best' evidence and selected for critical appraisal: Goverover, Y., Chiaravalloti, N., DeLuca, J. (2008). Reasons for selecting this study were:

- This study was considered "best evidence" out of the 5 studies researched.
- This study has an experimental and control group.
- There are multiple outcomes measured.
- This study is current.
- The treatment in the study was realistic and appropriate for the population which represents common practice with this population.

SUMMARY OF BEST EVIDENCE

Table 3: Description and appraisal of cohort study design by Goverover, Y., Chiaravalloti, N., DeLuca, J. (2008). Self-Generation to improve learning and memory of functional activities in persons with multiple sclerosis: meal preparation and managing finances. *Archives of Physical Medicine Rehabilitation*, 89, 1514-1521.

Aim/Objective of the Study/Systematic Review: To examine how memory and recall and performance of everyday tasks like meal preparation (eg., preparing breakfast foods) and managing finances (eg., paying an electric bill) is improved through a self-generation strategy in people with multiple sclerosis.

Study Design: This study is a cohort study design or a mixed-design with both a within- and between-subject factor.

Setting: The sample was conducted in clinics in the area. The study does not give a specific metropolitan or rural area.

Participants: The participants were recruited by advertisements that were given out at support groups and clinics in the area. An initial phone call was made to screen participants based on the inclusion and exclusion criteria. The exclusion criteria includes: (1) a history of another neurological illness besides MS, (2) a history of a major mental illness, (3) a history of alcohol or drug use, or (4) severe vision or motor deficit that may interfere with procedures in the study. The participants were interviewed and then tested after the phone call screen.

The sample size included 38 participants. The sample involved two separate groups of twenty participants with MS and a control group of eighteen healthy participants. The participants with MS had a diagnosis of MS according to the criteria of Poser et al. The healthy participants who were the control did not have reported neurological disabilities.

Sixteen participants had relapse remitting MS. Two participants had primary progressive MS and two participants had secondary progressive MS. All participants with MS were exacerbation free for one month and not using corticosteroids. The groups did not have a significant difference regarding age, sex, education, and intelligence before illness. There were no reported drop-outs in this sample. All participants who participated were paid at the end of the study.

Intervention Investigated: The participants participated in 3 hours of testing. The researchers delivered the intervention and the study took place at a non-profit rehabilitation research institution. During this time, the neuropsychologic battery and the self-generation protocol was administered. The study used Assessment of Motor and Process Skills (AMPS) for the meal preparation tasks. The managing finance tasks were broken down specifically for this study by using activity analysis and were looked over by an OT. A meal preparation task and a managing finance task were done in the provided condition. A meal preparation task and a managing finance task were done in the generated condition. A task from each area was shown in the provided condition where all instructions were included and participants read them. The other task was shown in a generated condition where the participants had to generate a word to fill in

the blank that coordinates with the step of the task. Two tasks were learned first by the participants.

Following the task presentations was immediate recall in that participants had to perform the tasks. Between the initial presentation and the performance recall of the task, participants' complete neuropsychological tests. This takes 30 minutes to do. The procedure was repeated and the participant learned the 2 other tasks.

Participants were contacted by phone one week after testing to examine the verbal recall of the material shown in the self-generation strategy. So, all four tasks were assessed for verbal recall of the task steps.

Outcome Measures: This study did provide the reader with a lot of outcome measures but the researchers did not justify their reliability and validity for all. Although, all of the measures mentioned below are standardized and all but the STAI and CMDI are widely used assessments of cognition. All outcome measures are included and explained in detail:

Weschler Adult Intelligence Scale-Revised (WAIS-R) digit span forward and backward trial: In the digit span forward trial, the participant must repeat, in the order stated by the examiner, a line of digits. For the digit span backward trial, the participant is asked to repeat the line of digits in a reverse order from the way they are presented. The number of responses that were correct on each trial was the dependent variable.

Symbol Digit Modalities Test (SDMT): This test involves a set of 9 geometric shapes and each one has a number from 1 to 9. A key is located at the top of page, which shows the number to correspond to the shape. Participants were shown the shape and they had to quickly say what the number was for that shape. The key was a reference for the participants. The number of correctly identified numbers to the shapes within 90 seconds was the dependent variable. The SDMT is valid and is able to measure the processing speed in people with MS.

Used three selected subtests of the Delis-Kaplan Executive Function System (D-KEFS):

(1) Trail-Making Test (TMT): The score of the switching task of numbers and letters was the dependent variable. This test looks at flexibility of thinking processes on a task that is visuomotor sequencing. The second dependent variable was the completion of the task in seconds.

(2) The Verbal Fluency Test: This test assesses fluid verbal production. Verbal generation of words are spoken in 60 seconds the letter initials of F, A, and S. The dependent variable is the number of words that are generated when the 3 letters are added up.

(3) Color-Word Interference Test: This test assess interference or shift perception when doing a know task of reading to a color-naming task that the examiner presents. The dependent variable is the amount of time in seconds to complete the switching attention task.

Boston Naming Test (BNT): The test displays 60 line drawings of objects that are common that participants must name. The BNT is an assessment that has been used on patients with the conditions of aphasia, dementia, and stroke and is able to identify deficits in patients. The amount of numbers that are correct is the dependent variable.

California Verbal Learning Test (CVLT): A list of 16 words is presented from 4 semantic categories. Each of the 16 items in the lists of the CVLT belongs to 1 of the 4 categories presented for shopping items. Over 5 trials, list A will be shown and followed by list B that has 16 words that will have only 1 trial. Delayed recall and recognition of the items in list A followed by an immediate recall for list B. The performance was assessed for recognition of a target and/or distraction items at the delay period of 20 minutes. The discriminability and response bias of the CVLT were calculated.

State-Trait Anxiety Inventory (STAI): The STAI is standardized and is an established measure of anxiety. STAI state and trait scores that are higher show more anxiety.

Chicago Multiscale Depression Inventory (CMDI): This inventory is a self-report measure with 42 items that assesses depression in MS and other population conditions. The overall score was used as a measure for depressive symptomatology.

Main Findings: Refer to table 4: Neuropsychologic Test Performance

Table 4: Neuropsychologic Test Performance

Domain Assessed	MS (n=20)	Healthy Controls (n=18)	F	Effect Size
Speed of processing				
SDMT	47.3±12.9	46.2±14.3	0.06	.002
Episodic memory				
CVLT sum of 5 trials	54.6±10.6	58.7±8.1	1.7	.04
CVLT discriminability	94.2±7.5	94.6±5.0	0.05	.002
Working Memory				
Digit Span forward	9.7±2.6	11.0±2.0	3.1	.08
Digit Span backward	7.5±2.7	8.3±2.9	0.83	.02
Executive Functions				
D-KEFS TMT: number-letter switching	105.7±44.1	68.5±19.6	10.8†	.23
D-KEFS Verbal Fluency Test letter fluency	33.5±13.1	45.1±12.1	7.9†	.18
D-KEFS Color-Word Interference Test: inhibition & switching	73.1±29.9	56.6±15.1	4.3*	.11
Toglia category assessment	30.3±3.3	30.7±2.7	0.18	.005
Deductive reasoning test	18.8±1.6	19.6±1.3	2.8	.07
Language				
BNT	54.9±4.1	51.7±8.0	2.4	.06
Affect Symptomatology				
STAI state anxiety	35.1±13.2	30.6±7.9	1.6	.06
STAI trait anxiety	38.8±11.7	38.7±8.9	0.001	.001
CMDI	80.3±27.0	71.3±19.8	1.2	.03
NOTE. Values are mean ± SD or as otherwise indicated.				
*P<.05; †P<.01.				
*This table was copied from Goverover, Y., Chiaravalloti, N., DeLuca, J., 2008, pg. 1517				

Original Authors' Conclusions: The study concluded that "self-generation may hold substantial promise for improving the lives of persons with MS showing new learning and memory deficits" (pg. 1520).

Critical Appraisal:

Selection and data collection biases:

There is a sample/selection bias in that there might be a volunteer or referral bias. The participants may be more motivated to participate because they are more concerned with their health. This study has no PEDro score.

Limitations:

There were a relatively small number of participants with MS who did not have a long term course of MS with respect to cognitive deficits. The study would have been more robust if randomized when assigned learning conditions rather than alternating assignments. The tasks assigned may have been over learned and the participants could have used procedural memory to complete the tasks. Lastly, the study could have looked at the more long term results of recall for the patients with MS.

Validity:

The researchers were able to determine that people with MS were able to recall items during the self-generation task. Multiple outcome measures that were used in this study really only assessed cognition and psychological factors. The study did not use a measure to assess functional outcomes so what the participants learned may or may not have shown an improvement in their everyday activities. The tasks of meal preparation may be familiar as well, so they may already have improved results because of how comfortable they are with the task.

Interpretation of Results:

Neuropsychologic and Emotional Functioning: From the results of the cognitive portion of the neuropsychologic testing, participants with MS showed similar functioning as the control participants except for the D-KEFS. More specifically, the performance of the D-KEFS TMT took significantly longer for the MS group than the control group ($P = .002$). The MS group also generated a significant amount of fewer words for the D-KEFS Verbal Fluency test than the control participants ($P = .008$). Lastly, the D-KEFS Color-Word Interference Test required the MS group to take a more significant amount of time to complete than the control group ($P = .04$). The results of the emotional functioning scores showed to be in a normative range for both groups according to published normative data. The results of the neuropsychological tests are hard to determine if they are significant to the intervention that was presented because they were only done in one time period. The participants did not get retested by these same tests after the intervention to see if there was a difference. The writer is assuming that the researchers wanted to highlight what the cognitive areas of concern were to show that the intervention targeted the area.

Generation Effect: Self-generation showed a medium effect size for managing finances and meal preparation over provided presentations ($P < .001$). The difference between the MS group and the control group showed a small effect size within the conditions

that were provided and generated ($P = .61$). The control group benefited from immediate recall of self-generation ($P = .004$). The MS group benefited from the 1-week recall of self-generation ($P = .06$). There was a stronger effect on self-generation meal preparation task than the self-generation managing finance tasks for all participants ($P = .05$). This study shows that having a person generate words to fill in the blanks does improve recall when learning a task. The study also showed that when tasks are more familiar or more meaningful to the participant than the results can show a larger improvement. The intervention used in this study could be used as an OT treatment for clients with MS but with many other generated IADLs that clients may struggle with during their everyday activities. There could also be less outcome measures and a test/retest of some of them over a period of time to determine treatment effects on cognition.

Summary/Conclusion: Cognitive training is better than no treatment at all for people with MS but there is no one defined protocol that has been shown to be the most effective. Cognitive training refers to or is interpreted to mean many different protocols from self-generation to computer-based to paper and pencil tasks. The assumption is that these procedures translate to functional use in everyday life. This is a flawed assumption because the context of the person with MS is ignored. It is important to find out what is meaningful to the person in their life and to tailor the protocol(s) to the area of concern. This study was able to address two occupations but can the self-generation technique be applied to other occupations that are not as familiar to a person with MS, so that they are able to remember and learn a new task.

Table 5: Characteristics of included studies

	Study 1 Gentry, T. (2008) N = 20	Study 2 Vogt, A. et al. (2009) N = 45	Study 3 Tesar, N. et al. (2005) N = 19	Study 4 Shevil, E. & Finiayson, M. (2009) N = 35
Study design	Cohort design (2b)	Cohort design (2b)	Cohort design (2b)	Cohort/Qual. (2b/ NA)
Intervention Investigated	Computer-based training w/PDA	Computer-based training w/ <i>BrainStim</i>	Compensation strategies & program relevance in everyday life	Process evaluation of "Mind over Matter"
Outcomes used	CHART-R, COPM, RBMT-E, study checklist	Working memory (6), STM (2), Mental speed (2), Questionnaires (4) – (pg. 228)	MWT-B, VLT, NVLT, DAUF, CKV, HAWIE-R, BDI, MFIS, Follow-up questionnaire	MS Neuropsychological Screening Questionnaire, MSNQ, focus groups, Questionnaire for program eval., facilitators reflection notes
Findings	Using PDA significantly improved participants' functional performance in everyday life tasks; compensatory assistive tech.	Training leads to improvement in fatigue, working memory, & mental speed performance; home computer-based training can be modified to the MS patient's everyday agenda	Teach patients compensatory strategies that can transfer to everyday lives	A self-management program addresses cogn. changes in MS, feasible, and potentially beneficial for clients w/ mild to mod. symptoms; compensatory strategies, education discussion about cogn. symptoms and how person w/MS is affected

IMPLICATIONS FOR PRACTICE: OT practitioners do not have a single clear strategy for providing cognitive rehabilitation to their clients with MS. The research has varying procedures and protocols that may not necessarily be transferable to everyday life. An article done by O'Brien, A. R. et al. conducted a review of evidence-based studies that looked at cognitive rehabilitation in people with MS to recommend interventions in this area. The different techniques that the researchers found were: computer-assisted programs; calendars, notebooks, diaries, and lists; metacognition therapy; generation effect; repetition effect; memory notebooks; story memory technique; communication skills and etc. The researchers looked at 4 different areas of cognition which included attention, executive functioning, learning and memory, and nonspecific cognitive rehabilitation interventions. The researchers expressed that no recommendations could be given at this time and that further research is needed for all of the areas except for learning and memory. In the learning and memory area, a study showed a possible program intervention by using a story memory technique. Four other studies are summarized in table 5 that show a couple of interventions that would be beneficial and others that will need further research.

Study 1 did find that PDAs did show a statistically significant effect on cognition and mobility scales of the Craig Handicap Assessment and Rating Technique-Revised (CHART-R). Using a PDA improved cognition for people with MS while doing their everyday activities. Study 2 was a computer-based training program that looked at how a high intensity training and distributed training affected working memory in people with MS. They were able to show that there were improved fatigue symptoms, working memory, and mental speed performances. The study did not specifically identify though how any of these functions could increase functional outcomes for people with MS, so the evidence on if this should be a good cognitive training technique is unknown. The study does not specify if the training would transfer over to functional everyday tasks.

Study 3 and 4 both talked about compensatory strategies that could be used in everyday life. Study 3 explained that they were going to address the two most severe cognitive areas and help the participant to use a compensatory technique in everyday tasks for people with MS. They did not specify or say how they would apply a cognitive compensatory technique to an everyday task like remembering when to take medication or how they were going to plan their day out if they had several errands to run. Study 4 looked at "*Mind Over Matter*" to see if the program is beneficial to people with MS. In this study, people with MS were able to identify their level of cognitive difficulties and were able to use compensatory strategies that the program taught them to function in their environment. A program like this one could really increase awareness not only to the client with MS but to the family as well.

EDUCATION: As OT practitioners we should know the current evidence-based literature on cognitive rehabilitation for people with MS and identify what protocols or techniques work. OTs must also take into consideration what the results of the studies show so that they can justify the protocols effectiveness in everyday activities. Practitioners may not know if the protocol is transferable to ADLs but they may be able to determine this if the study was able to do an intervention that included a cognitive treatment that included an ADL. This may be compared to computer-based training that may only be working on cognitive processes and has no transference to ADLs.

FUTURE RESEARCH: Future research needs to look at the transferability of cognitive rehabilitation to everyday activities for people with MS by doing a cognitive technique and then applying to an ADL. Future outcome measures should not only include cognitive assessments but also functional assessments like the Kitchen Task Assessment (KTA) or the Assessment of Motor and Process Skills (AMPS). Other assessments that could be used are the Canadian Occupational Performance Measure (COPM), the Craig Handicap Assessment and Rating Technique-Revised (CHART-R), and the Rivermead Behavioural Memory Test Extended (RBMT-E). Study 1 did use these assessments so hopefully other researchers will use them as well. Studies could also focus on the contextual nature of training by incorporating meaningful occupations that a person with MS need to be able to do so that the client is safe in his/ her environment that they function in.

There are many other future implications for cognitive rehabilitation in patients with multiple sclerosis. Possible ideas to research further include the level of impairment; interventions for specific cognitive impairments; looking into other areas like TBI and CVA who have some existing cognitive rehabilitation treatments; communication between clinical researchers and clinical practitioners for investigating treatment protocols; and long term benefits for clients with MS. More research is needed to determine the functional outcomes of cognitive rehabilitation for individuals with MS.

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